Figure 1

```
SEQ ID NO:
 6   mouse_E3αII   MASEMEPEVQ  AID-RSLLEC  SAEEIAGRWL  QATDLNREVY  QHLAHCVPKI   49
 4   human_E3αII   MASELEPEVQ  AID-RSLLEC  SAEEIAGKWL  QATDLTREVY  QHLAHYVPKI   49
15   mouse_E3αI    MADEEMDGAE  RMDVSPEPPL  APQRPASWWD  QQVDFYTAFL  HHLAQLVPEI   50
 2   human_E3αI    MADEEAGGTE  RMEISAELPQ  TPQRLASWWD  QQVDFYTAFL  HHLAQLVPEI   50
     Consensus     MA.E......  ..D....L..  .....A..W.  Q..D......  .HLA..VP.I   50


 6   mouse_E3αII   YCRGPNPFPQ  KEDTLAQHIL  LGPMEWYICA  EDPALGFPKL  EQANKPSHLC   99
 4   human_E3αII   YCRGPNPFPQ  KEDMLAQHVL  LGPMEWYLCG  EDPAFGFPKL  EQANKPSHLC   99
15   mouse_E3αI    YFAEMDPDLE  KQEESVQMSI  LTPLEWYLFG  EDPDICLEKL  KHSG-AFQLC   99
 2   human_E3αI    YFAEMDPDLE  KQEESVQMSI  FTPLEWYLFG  EDPDICLEKL  KHSG-AFQLC   99
     Consensus     Y.....P...  K.....Q...  L.P.EWYL.G  EDP.....KL  .......LC  100


 6   mouse_E3αII   GRVFKVGEPT  YSCRDCAVDP  TCVLCMECFL  GSIHRDHRYR  MTTSGGGGFC  149
 4   human_E3αII   GRVFKVGEPT  YSCRDCAVDP  TCVLCMECFL  GSIHRDHRYR  MTTSGGGGFC  149
15   mouse_E3αI    GKVFKSGETT  YSCRDCAIDP  TCVLCMDCFQ  SSVHKNHRYK  MHTSTGGGFC  149
 2   human_E3αI    GRVFKSGETT  YSCRDCAIDP  TCVLCMDCFQ  DSVHKNHRYK  MHTSTGGGFC  149
     Consensus     GRVFK.GE.T  YSCRDCA.DP  TCVLCM.CF.  .S.H..HRY.  M.TS.GGGFC  150


 6   mouse_E3αII   DCGDTEAWKE  GPYCQKHKLS  SSEVVEEEDP  LVHLSEDVIA  RTYNIFAIMF  199
 4   human_E3αII   DCGDTEAWKE  GPYCQKHELN  TSEIEEEEDP  LVHLSEDVIA  RTYNIFAITF  199
15   mouse_E3αI    DCGDTEAWKT  GPFCVDHEPG  RAGTTKESLH  -CPLNEEVIA  QARRIFPSVI  198
 2   human_E3αI    DCGDTEAWKT  GPFCVNHEPG  RAGTIKENSR  -CPLNEEVIV  QARKIFPSVI  198
     Consensus     DCGDTEAWK.  GP.C..HE..  ......E...  ...L.E.VIA  ....IF....  200


 6   mouse_E3αII   RYAVDILTWE  KESELPEDLE  VAEKSDTYYC  MLFNDEVHTY  EQVIYTLQKA  249
 4   human_E3αII   RYAVEILTWE  KESELPADLE  MVEKSDTYYC  MLFNDEVHTY  EQVIYTLQKA  249
15   mouse_E3αI    KYIVEMTIWE  EEKELPPELQ  IREKNERYYC  VLFNDEHHSY  DHVIYSLQRA  248
 2   human_E3αI    KYVVEMTIWE  EEKELPPELQ  IREKNERYYC  VLFNDEHHSY  DHVIYSLQRA  248
     Consensus     .Y.VE...WE  .E.ELP..L.  ..EK...YYC  .LFNDE.H.Y  ..VIY.LQ.A  250


 6   mouse_E3αII   VNCTQKEAIG  FATTVDRDGR  RPVRYGDFQY  CDQAKTVIVR  NTSRQTK-PL  298
 4   human_E3αII   VNCTQKEAIG  FATTVDRDGR  RSVRYGDFQY  CEQAKSVIVR  NTSRQTK-PL  298
15   mouse_E3αI    LDCELAEAQL  HTTAIDKEGR  RAVKAGVYAT  CQEAKEDIKS  HSENVSQHPL  298
 2   human_E3αI    LDCELAEAQL  HTTAIDKEGR  RAVKAGAYAA  CQEAKEDIKS  HSENVSQHPL  298
     Consensus     ..C...EA..  ...T..D..GR  R.V..G....  C..AK..I..  ........PL  300


 6   mouse_E3αII   KVQVMHSSVA  AHQNFGLKAL  SWLGSVIGYS  DGLRRILCQV  GLQEGPDGEN  348
 4   human_E3αII   KVQVMHSSIV  AHQNFGLKLL  SWLGSIIGYS  DGLRRILCQV  GLQEGPDGEN  348
15   mouse_E3αI    HVEVLHSVVM  AHQKFALRLG  SWMNKIMSYS  SDFRQIFCQA  CLVEEPGSEN  348
 2   human_E3αI    HVEVLHSEIM  AHQKFALRLG  SWMNKIMSYS  SDFRQIFCQA  CLREEPDSEN  348
     Consensus     .V.V.HS...  AHQ.F.L.L.  SW...I..YS  ...R.I.CQ.  .L.E.PD.EN  350


 6   mouse_E3αII   SSLVDRLMLN  DSKLWKGARS  VYHQLFMSSL  LMDLKYKKLF  ALRFAKNYRQ  398
 4   human_E3αII   SSLVDRLMLS  DSKLWKGARS  VYHQLFMSSL  LMDLKYKKLF  AVRFAKNYQQ  398
15   mouse_E3αI    PCLISRLMLW  DAKLYKGARK  ILHELIFSSF  FMEMEYKKLF  AMEFVKYYKQ  398
 2   human_E3αI    PCLISRLMLW  DAKLYKGARK  ILHELIFSSF  FMEMEYKKLF  AMEFVKYYKQ  398
     Consensus     ..L..RLML.  D.KL.KGAR.  ..H.L..SS.  .M...YKKLF  A..F.K.Y.Q  400


 6   mouse_E3αII   LQRDFMEDDH  ERAVSVTALS  VQFFTAPTLA  RMLLTEENLM  TVIIKAFMDH  448
 4   human_E3αII   LQRDFMEDDH  ERAVSVTALS  VQFFTAPTLA  RMLITEENLM  SIIIKTFMDH  448
15   mouse_E3αI    LQKEYISDDH  ERSISITALS  VQMLTVPTLA  RHLIEEQNVI  SVITETLLEV  448
 2   human_E3αI    LQKEYISDDH  DRSISITALS  VQMFTVPTLA  RHLIEEQNVI  SVITETLLEV  448
     Consensus     LQ.....DDH  ER..S.TALS  VQ.FT.PTLA  R.LI.E.N..  SVI..T...  450
```

Figure 1 (continued)

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SEQ ID NO:
6    mouse_E3αII   LKHRDAQGRF QFERYTALQA FKFRRVQSLI LDLKYVLISK PTEWSDELRQ   498
4    human_E3αII   LRHRDAQGRF QFERYTALQA FKFRRVQSLI LDLKYVLISK PTEWSDELRQ   498
15   mouse_E3αI    LPEYLDRNN- KFN-FQGYSQ DKLGRVYAVI CDLKYILISK PVIWTERLRA   496
2    human_E3αI    LPEYLDRNN- KFN-FQGYSQ DKLGRVYAVI CDLKYILISK PTIWTERLRM   496
     Consensus     L......... .F........ .K..RV...I .DLKY.LISK PT.W...LR.   500


6    mouse_E3αII   KFLQGFDAFL ELLKCMQGMD PITRQVGQHI EMEPEWEAAF TLQMKLTHVI   548
4    human_E3αII   KFLEGFDAFL ELLKCMQGMD PITRQVGQHI EMEPEWEAAF TLQMKLTHVI   548
15   mouse_E3αI    QFLEGFRSFL KILTCMQGME EIRRQVGQHI EVDPDWEAAI AIQMQLKNIL   546
2    human_E3αI    QFLEGFRSFL KILTCMQGME EIRRQVGQHI EVDPDWEAAI AIQMQLKNIL   546
     Consensus     .FLEGF..FL ..L.CMQGM. .I.RQVGQHI E...P.WEAA. ..QM.L....   550


6    mouse_E3αII   SMVQDWCALD EKVLIEAYKK CLAVLTQCHG GFTDGEQPIT LSICGHSVET   598
4    human_E3αII   SMMQDWCASD EKVLIEAYKK CLAVLMQCHG GYTDGEQPIT LSICGHSVET   598
15   mouse_E3αI    LMFQEWCACD EDLLLVAYKE CHKAVMRCST NFMSSTKTV- VQLCGHSLET   595
2    human_E3αI    LMFQEWCACD EELLLVAYKE CHKAVMRCST SFISSSKTV- VQSCGHSLET   595
     Consensus     :M.Q.WCA.D E..L..AYK. C....M.C.. .F........ ...CGHS.ET   600


6    mouse_E3αII   IRYCVSQEKV SIHLPISRLL AGLHVLLSKS EVAYKFPELL PLSELSPPML   648
4    human_E3αII   IYCVSQEKV SIHLPVSRLL AGLHVLLSKS EVAYKFPELL PLSELSPPML   648
15   mouse_E3αI    KSYKVSEDLV SIHLPLSRTL AGLHVRLSRL GAISRLHEFV PFDSFQVEVL   645
2    human_E3αI    KSYRVSEDLV SIHLPLSRTL AGLHVRLSRL GAVSRLHEFV SFEDFQVEVL   645
     Consensus     ..Y.VS...V SIHLP.SR.L AGLHV.LS.. .......E.. P.......L   650


6    mouse_E3αII   IEHPLRCLVL CAQVHAGMWR RNGFSLVNQI YYYHNVKCRR EMFDKDIVML   698
4    human_E3αII   IEHPLRCLVL CAQVHAGMWR RNGFSLVNQI YYYHNVKCRR EMFDKDVVML   698
15   mouse_E3αI    VEYPLRCLVL VAQVVAEMWR RNGLSLISQV FYYQDVKCRE EMYDKDIIML   695
2    human_E3αI    VEYPLRCLVL VAQVVAEMWR RNGLSLISQV FYYQDVKCRE EMYDKDIIML   695
     Consensus     .E.PLRCLVL .AQV.A.MWR RNG.SL..Q. .YY..VKCR. EM.DKDI.ML   700


6    mouse_E3αII   QTGVSMMDPN HFLMIMLSRF ELYQLFSTPD YGKRFSSEVT HKDVVQQNNT   748
4    human_E3αII   QTGVSMMDPN HFLMIMLSRF ELYQIFSTPD YGKRFSSEIT HKDVVQQNNT   748
15   mouse_E3αI    QIGASIMDPN KFLLLVLQRY EL-----TDA FNKTIST--K DQDLIKQYNT   738
2    human_E3αI    QIGASLMDPN KFLLLVLQRY EL-----AEA FNKTIST--K DQDLIKQYNT   738
     Consensus     Q.G.S.MDPN .FL...L.R. EL.....T.. ..K..S.... ..D...Q.NT   750


6    mouse_E3αII   LIEEMLYLII MLVGERFNPG VGQVAATDEI KREIIHQLSI KPMAHSELVK   798
4    human_E3αII   LIEEMLYLII MLVGERFSPG VGQVNATDEI KREIIHQLSI KPMAHSELVK   798
15   mouse_E3αI    LIEEMLQVLI YIVGERYVPG VGNVTREEVI MREITHLLCI EPMPHSAIAR   788
2    human_E3αI    LIEEMLQVLI YIVGERYVPG VGNVTKEEVT MREIIHLLCI EPMPHSAIAK   788
     Consensus     LIEEML...I ..VGER..PG VG.V.....I .REIIH.L.I .PM.HS...K   800


6    mouse_E3αII   SLPEDENKET GMESVIESVA HFKKPGLTGR GMYELKPECA KEFNLYFYHF   848
4    human_E3αII   SLPEDENKET GMESVIEAVA HFKKPGLTGR GMYELKPECA KEFNLYFYHF   848
15   mouse_E3αI    NLPENENNET GLENVINKVA TFKKPGVSGH GVYELKDESL KDFNMYFYHY   838
2    human_E3αI    NLPENENNET GLENVINKVA TFKKPGVSGH GVYELKDESL KDFNMYFYHY   838
     Consensus     .LPE.EN.ET G.E.VI..VA .FKKPG..G. G.YELK.E.. K.FN.YFYH.   850


6    mouse_E3αII   SRAEQSKAEE AQRKLKRENK EDTALPPPAL PPFCPLFASL VNILQCDVML   898
4    human_E3αII   SRAEQSKAEE AQRKLKRQNR EDTALPPPVL PPFCPLFASL VNILQSDVML   898
15   mouse_E3αI    SKTQHSKAEH MQKKRRKQEN KDEALPPPPP PEFCPAFSKV VNLLSCDVMI   888
2    human_E3αI    SKTQHSKAEH MQKKRRKQEN KDEALPPPPP PEFCPAFSKV INLLNCDIMM   888
     Consensus     S....SKAE. .Q.K...Q.. .D.ALPPP.. P.FCP.F... VN.L.CDVM.   900
```

Figure 1 (continued)

```
SEQ ID NO:
6    mouse_E3αII   YIMGTILQWA  VEHHGSAWSE  SMLQRVLHLI  GMALQEEKHH  LENAVEGHVQ   948
4    human_E3αII   CIMGTILQWA  VEHNGYAWSE  SMLQRVLHLI  GMALQEEKQH  LENVTEEHVV   948
15   mouse_E3αI    YILRTIFERA  VDTESNLWTE  GMLQMAFHIL  ALGLLEEKQQ  LQKAPEEEV-   937
2    human_E3αI    YILRTVFERA  IDTDSNLWTE  GMLQMAFHIL  ALGLLEEKQQ  LQKAPEEEV-   937
     Consensus     YI..TI...A  V......W.E  .MLQ...H..  ...L.EEKQ.  L..A.EE.V.   950


6    mouse_E3αII   TFTFTQKISK  PGDAPHNSPS  ILAMLETLQN  APSLEAHKDM  IRWLLKMFNA   998
4    human_E3αII   TFTFTQKISK  PGEAPKNSPS  ILAMLETLQN  APYLEVHKDM  IRWILKTFNA   998
15   mouse_E3αI    AFDFYHKASR  LGSSAMNAQN  IQMLLERLKG  IPQLEGQKDM  ITWILQMFDT   987
2    human_E3αI    TFDFYHKASR  LGSSAMNIQM  L---LEKLKG  IPQLEGQKDM  ITWILQMFDT   984
     Consensus     TF.F..K.S.  .G....N...  I...LE.L..  .P.LE..KDM  I.WIL.MF..  1000


6    mouse_E3αII   IKKIRE--CS  SSSPVAEAEG  TIMEESSRDK  DKAERKRKAE  IARLRREKIM  1046
4    human_E3aII   VKKMRE--SS  PTSPVAETEG  TIMEESSRDK  DKAERKRKAE  IARLRREKIM  1046
15   mouse_E3αI    VKRLREKSCL  VVATTSGLEC  IKSEEITHDK  EKAERKRKAE  AARLHRQKIM  1037
2    human_E3αI    VKRLREKSCL  IVATTSGSES  IKNDEITHDK  EKAERKRKAE  AARLHRQKIM  1034
     Consensus     VK..RE..C.  ........E.  ...EE...DK  .KAERKRKAE  .ARL.R.KIM  1050


6    mouse_E3αII   AQMSEMQRHF  IDENKELFQQ  TLELDTSASA  TL--DSSPPV  SDAALTALGP  1094
4    human_E3αII   AQMSEMQRHF  IDENKELFQQ  TLELDASTSA  VL--DHSPVA  SDMTLTALGP  1094
15   mouse_E3αI    AQMSALQKNF  IETHKLMYDN  TSEVTGKEDS  IMEEESTSAV  SEASRIALGP  1087
2    human_E3αI    AQMSALQKNF  IETHKLMYDN  TSEMPGKEDS  IMEEESTPAV  SDYSRIALGP  1084
     Consensus     AQMS..Q..F  I...K.....  T.E.......  .....S.P.V  SD....ALGP  1100


6    mouse_E3αII   AQTQVPEPRQ  FVTCILCQEE  QEVTVGSRAM  VLAAFVQRST  VLSKDRTKTI  1144
4    human_E3αII   TQTQVPEQRQ  FVTCILCQEE  QEVKVESRAM  VLAAFVQRST  VLSKNRSKFI  1144
15   mouse_E3αI    KRGPAVTEKE  VLTCILCQEE  QEVKLENNAM  VLSACVQKST  ALTQHRGKPV  1137
2    human_E3α     KRGPSVTEKE  VLTCILCQEE  QEVKIENNAM  VLSACVQKST  ALTQHRGKPI  1134
     Consensus     ..........  ..TCILCQEE  QEVK.E..AM  VL.A.VQ.ST  .L...R.K.I  1150


6    mouse_E3αII   AD-PEKYDPL  FMHPDLSCGT  HTGSCGHVMH  AHCWQRYFDS  VQAKEQRRQQ  1193
4    human_E3αII   QD-PEKYDPL  FMHPDLSCGT  HTSSCGHIMH  AHCWQRYFDS  VQAKEQRRQQ  1193
15   mouse_E3αI    DHLGETLDPL  FMDPDLAHGT  YTGSCGHVMH  AVCWQKYFEA  VQ---LSSQQ  1184
2    human_E3αI    ELSGEALDPL  FMDPDLAYGT  YTGSCGHVMH  AVCWQKYFEA  VQ---LSSQQ  1181
     Consensus     ....E..DPL  FM.PDL..GT  .TGSCGHVMH  A.CWQ.YF..  VQ......QQ  1200


6    mouse_E3αII   RLRLHTSYDV  ENGEFLCPLC  ECLSNTVIPL  L-LPPRSILS  RRLN-FSDQP  1241
4    human_E3αII   RLRLHTSYDV  ENGEFLCPLC  ECLSNTVIPL  L-LPPRNIFN  NRLN-FSDQP  1241
15   mouse_E3αI    RIHVDL-FDL  ESGEYLCPLC  KSLCNTVIPI  IPLQPQKINS  ENAEALAQLL  1233
2    human_E3αI    RIHVDL-FDL  ESGEYLCPLC  KSLCNTVIPI  IPLQPQKINS  ENADALAQLL  1230
     Consensus     R......D.  E.GE.LCPLC  ..L.NTVIP.  ..L.P..I.S  ..........  1250


6    mouse_E3αII   DLAQWTRAVT  QQIKVVQMLR  RKHNAA-DTS  SSEDTEAMNI  IPIPEGFRPD  1290
4    human_E3αII   NLTQWIRTIS  QQIKALQFLR  KEESTP-NNA  STKNSENVDE  LQLPEGFRPD  1290
15   mouse_E3αI    TLARWIQTVL  ARISGYNIKH  AKGEAPAVPV  LFNQGMGDST  FEFHSILSFG  1283
2    human_E3αI    TLARWIQTVL  ARISGYNIRH  AKGENP-IPI  FFNQGMGDST  LEFHSILSFG  1279
     Consensus     .LA.WI.TV.  ..I.......  .K...P-...  ..........  ..........  1300


6    mouse_E3αII   FYPRNPYSDS  IKEMLTTFGT  AAYKVGLKVH  PNEGDPRVPI  LCWGTCAYTI  1340
4    human_E3αII   FRPKIPYSES  IKEMLTTFGT  ATYKVGLKVH  PNEEDPRVPI  MCWGSCAYTI  1340
15   mouse_E3αI    VQSSVKYSNS  IKEMVILFAT  TIYRIGLKVP  PDELDPRVPM  MTWSTCAFTI  1333
2    human_E3αI    VESSIKYSNS  IKEMVILFAT  TIYRIGLKVP  PDERDPRVPM  LTWSTCAFTI  1329
     Consensus     ......YS.S  IKEM...F.T  ..Y..GLKV.  P.E.DPRVP.  ..W.TCA.TI  1350
```

Figure 1 (continued)

```
SEQ ID NO:
6    mouse_E3αII   QSIERILSDE EKPVFGPLPC RLDDCLRSLT RFAAAHWTVA LLPVVQGHFC 1390
4    human_E3αII   QSIERILSDE DKPLFGPLPC RLDDCLRSLT RFAAAHWTVA SVSVVQGHFC 1390
15   mouse_E3αI    QAIENLLGDE GKPLFGALQN RQHSGLKALM QFAVAQRATC PQVLIHKHLA 1383
2    human_E3αI    QAIENLLGDE GKPLFGALQN RQHNGLKALM QFAVAQRITC PQVLIQKHLV 1379
     Consensus     Q.IE..L.DE .KPLFG.L.. R....L..L. .FA.A..... .....Q.H.. 1400


6    mouse_E3αII   KLFASLVPSD SYEDLPCILD IDMFHLLVGL VLAFPALQCQ D---FSGSSL 1437
4    human_E3αII   KLFASLVPND SHEELPCILD IDMFHLLVGL VLAFPALQCQ D---FSGISL 1437
15   mouse_E3αI    RLLSVILPNL QSENTPGLLS VDLFHVLVGA VLAFPSLYWD DTVDLQPSPL 1433
2    human_E3αI    RLLSVVLPNI KSEDTPCLLS IDLFHVLVGA VLAFPSLYWD DPVDLQPSSV 1429
     Consensus     .L.....PN. ..E..PC.L. ID.FH.LVG. VLAFP.L... D......SSL 1450


6    mouse_E3αII   ATG--DLHIF HLVTMAHIVQ ILLTSCTEEN ---GMDQENP TGEEELAILS 1482
4    human_E3αII   GTG--DLHIF HLVTMAHIIQ ILLTSCTEEN ---GMDQENP PCEEESAVLA 1482
15   mouse_E3αI    SSSYNHLYLF HLITMAHMLQ ILLTTDTDLS PGPPLAEGEE DSEEARCASA 1483
2    human_E3αI    SSSYNHLYLF HLITMAHMLQ ILLTVDTGL- ---PLAQVQE DSEEAHSASS 1475
     Consensus     ......L..F HL.TMAH..Q ILLT..T... ---...Q... ..EE...... 1500


6    mouse_E3αII   LHKTLHQYTG SALKEAPSGW HLWRSVRAAI MPFLKCSALF FHYLNGVPAP 1532
4    human_E3αII   LYKTLHQYTG SALKEIPSGW HLWRSVRAGI MPFLKCSALF FHYLNGVPSP 1532
15   mouse_E3αI    FFVEVSQHTD GLTGCGAPGW YLWLSLRNGI TPYLRCAALL FHYLLGVAPP 1533
2    human_E3αI    FFAEISQYTS GSIGCDIPGW YLWVSLKNGI TPYLRCAALF FHYLLGVTPP 1525
     Consensus     ......QYT. ........GW .LW.S.R.GI .P.L.C.ALF FHYL.GV..P 1550


6    mouse_E3αII   PDLQV-SGTS HFEHLCNYLS LPTNLIHLFQ ENSDIMNSLI ESWCQNSEVK 1581
4    human_E3αII   PDIQV-PGTS HFEHLCSYLS LPNNLICLFQ ENSEIMNSLI ESWCRNSEVK 1581
15   mouse_E3αI    EELFANSAEG EFSALCSYLS LPTNLFLLFQ EYWDTIRPLL QRWCGDPALL 1583
2    human_E3αI    EELHTNSAEG EYSALCSYLS LPTNLFLLFQ EYWDTVRPLL QRWCADPALL 1575
     Consensus     ..L...S... .F..LCSYLS LPTNL..LFQ E..D....L. ..WC...... 1600


6    mouse_E3αII   RYLNGERGAI SYPRGANKLI DLPEDYSSLI NQASNFSCPK SGGDKSRAPT 1631
4    human_E3αII   RYLEGERDAI RYPRESNKLI NLPEDYSSLI NQASNFSCPK SGGDKSRAPT 1631
15   mouse_E3αI    KSLKQKSAVV RYPRKRNSLI ELPEDYSCLL NQASHFRCPR SADDERKHPV 1633
2    human_E3αI    NCLKQKNTVV RYPRKRNSLI ELPDDYSCLL NQASHFRCPR SADDERKHPV 1625
     Consensus     ..L....... RYPR..N.LI .LPEDYS.L. NQAS.F.CP. S..D....P. 1650


6    mouse_E3αII   LCLVCGSLLC SQSYCCQAEL EGEDVGACTA HTYSCGSGAG IFLRVRECQV 1681
4    human_E3αII   LCLVCGSLLC SQSYCCQTEL EGEDVGACTA HTYSCGSGVG IFLRVRECQV 1681
15   mouse_E3αI    LCLFCGAILC SQNICCQEIV NGEEVGACVF HALHCGAGVC IFLKIRECRV 1683
2    human_E3αI    LCLFCGAILC SQNICCQEIV NGEEVGACIF HALHCGAGVC IFLKIRECRV 1675
     Consensus     LCL.CG..LC SQ..CCQ... .GE.VGAC.. H...CG.GV. IFL..REC.V 1700


6    mouse_E3αII   LFLAGKTKGC FYSPPYLDDY GETDQGLRRG NPLHLCQERF RKIQKLWQQH 1731
4    human_E3αII   LFLAGKTKGC FYSPPYLDDY GETDQGLRRG NPLHLCKERF KKIQKLWHQH 1731
15   mouse_E3αI    VLVEGKARGC AYPAPYLDEY GETDPGLKRG NPLHLSRERY RKLHLVWQQH 1733
2    human_E3αI    VLVEGKARGC AYPAPYLDEY GETDPGLKRG NPLHLSRERY RKLHLVWQQH 1725
     Consensus     ....GK..GC .Y..PYLD.Y GETD.GL.RG NPLHL..ER. RK....WQQH 1750


6    mouse_E3αII   SITEEIGHAQ EANQTLVGID WQHL        1755
4    human_E3αII   SVTEEIGHAQ EANQTLVGID WQHL        1755
15   mouse_E3αI    CIIEEIARSQ ETNQMLFGFN WQLL        1757
2    human_E3αI    CIIEEIARSQ ETNQMLFGFN WQLL        1749
     Consensus     .I.EEI...Q E.NQ.L.G.. WQ.L        1774
```

Figure 2

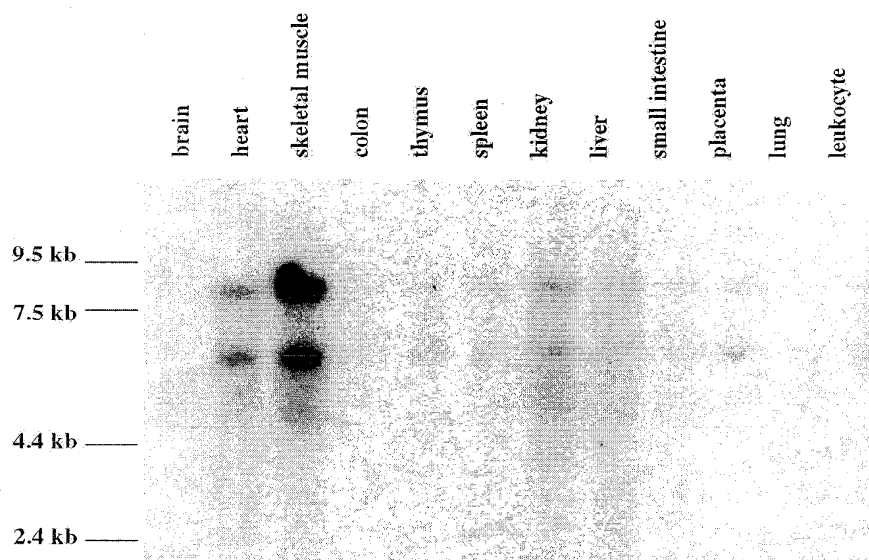**The Expression Profile of huE3α-II in Human Tissues**

Figure 3
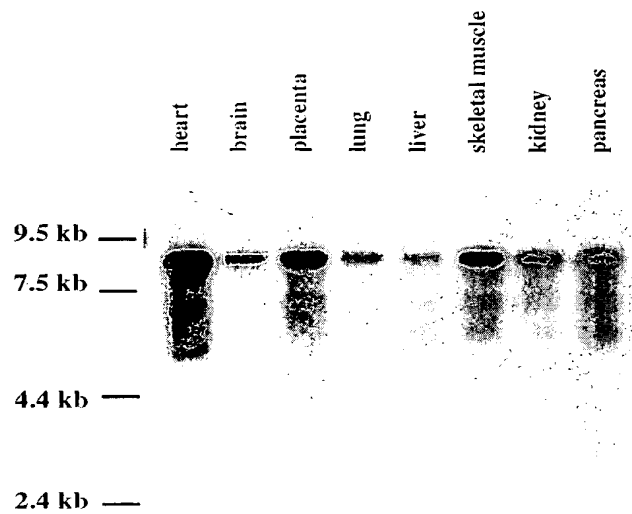
The Expression Profile of huE3α-I in Human Tissues

heart brain placenta lung liver skeletal muscle kidney pancreas

9.5 kb ——

7.5 kb ——

4.4 kb ——

2.4 kb ——

Figure 4- Ubiquitination of Endogenous Proteins

Ubiquitin–α– 125I- Lactalbumin- Conjugates
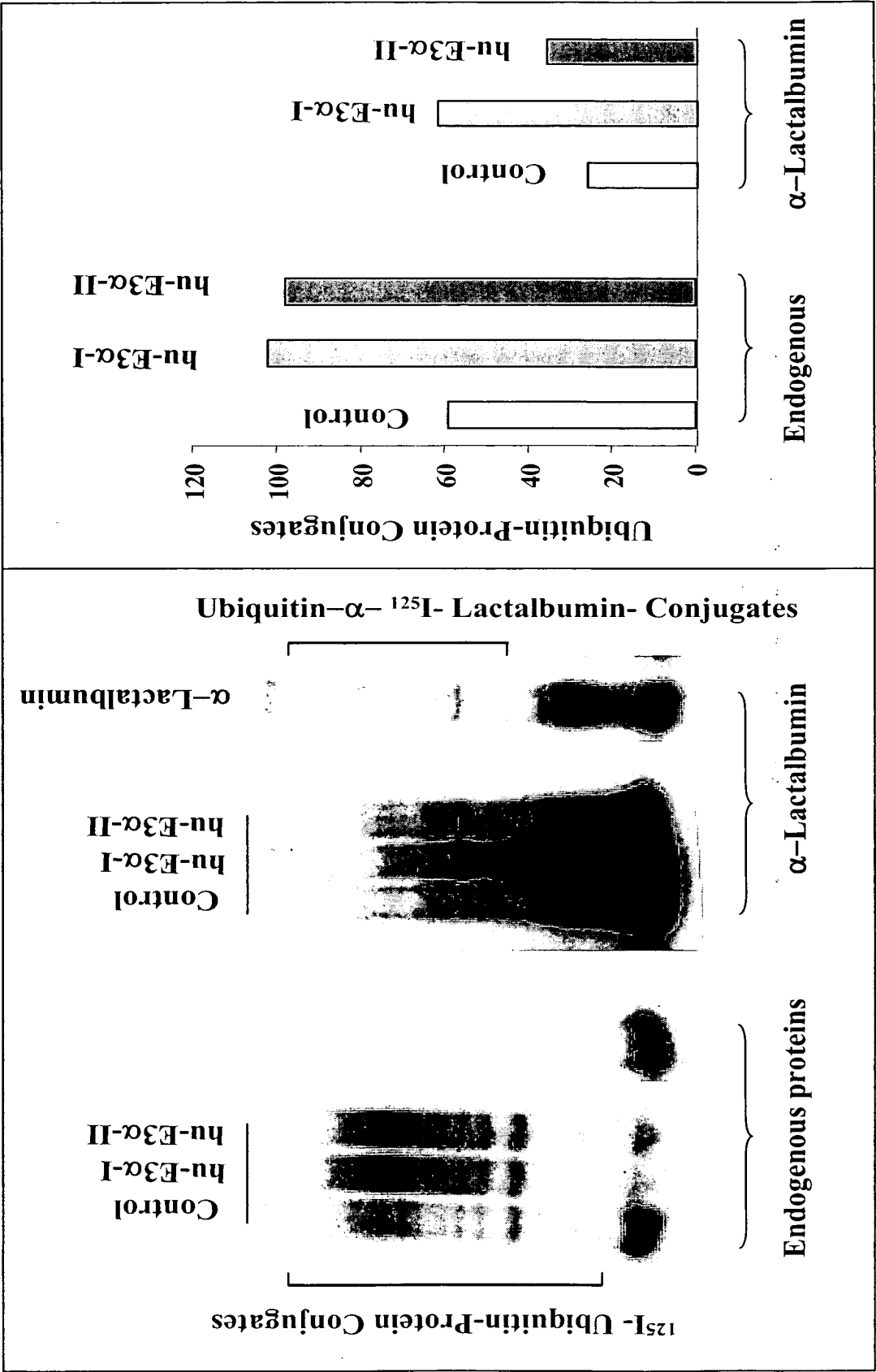
Figure 5

Transfection of Human E3a-I or E3a-II cDNA Stimulates
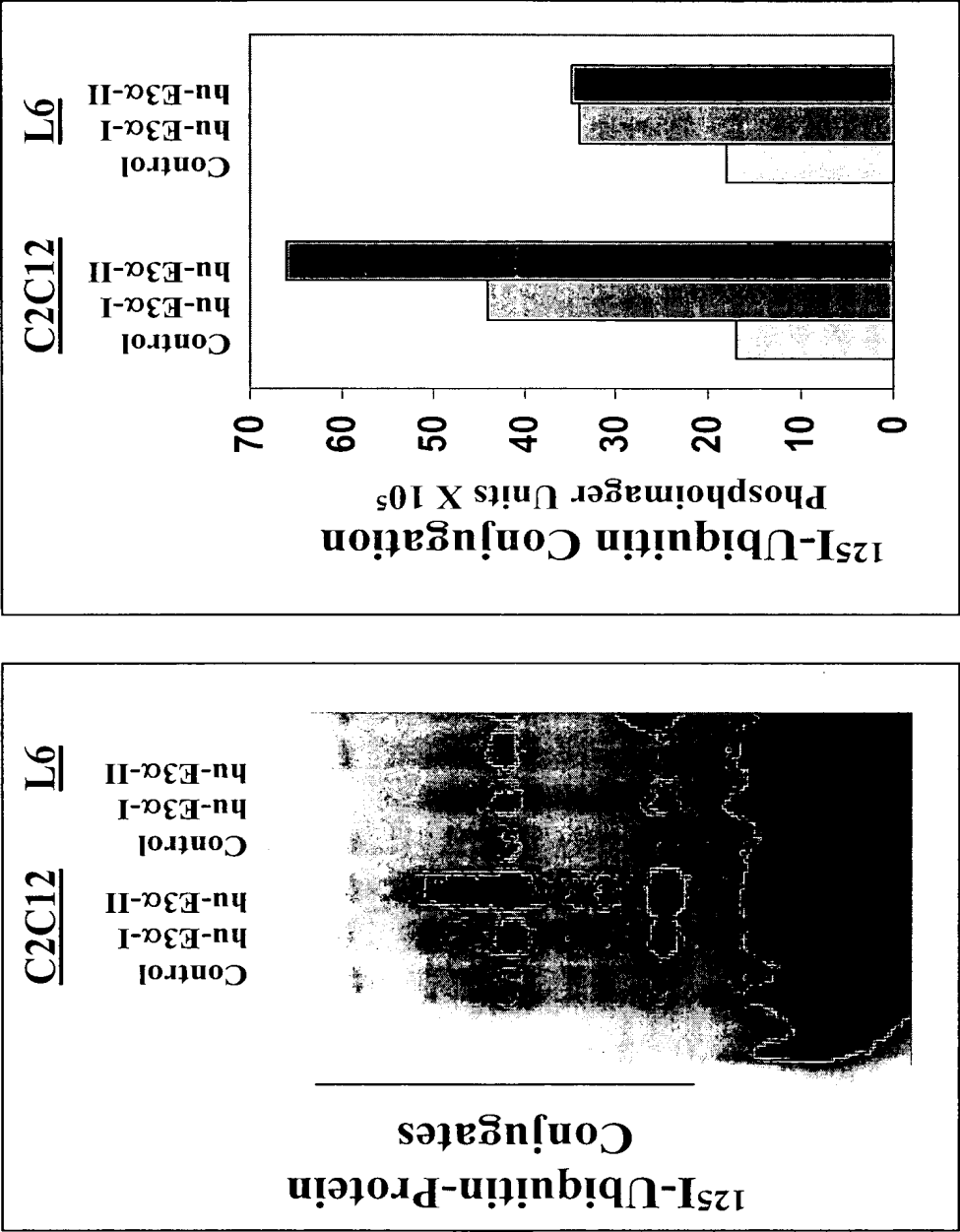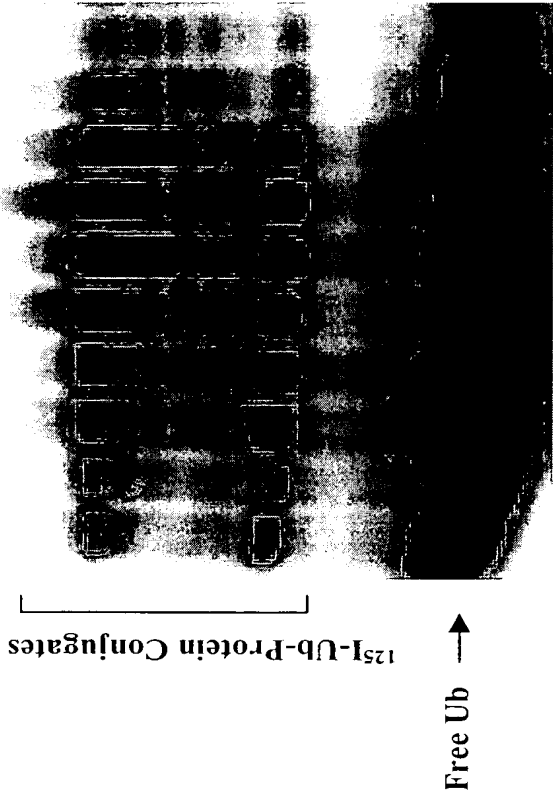Ubiquitin Conjugation in Cultured Muscle Cell Lines

Figure 6 ^{125}I-Ubiquitin Conjugation to Muscle Proteins and Its Sensitivity to E3α Inhibitor in Skeletal Muscle Extracts

Figure 7

Rates of Ubiquitination of N-end Rule Substrate α-Lactalbumin in Skeletal Muscle Extracts

Control v.s. 5 Day-Tumor-Bearing

^{125}I-Lactalbumin_Ub Conjugates

Control v.s. 3 Day-Tumor-Bearing

^{125}I-Lactalbumin_Ub Conjugates
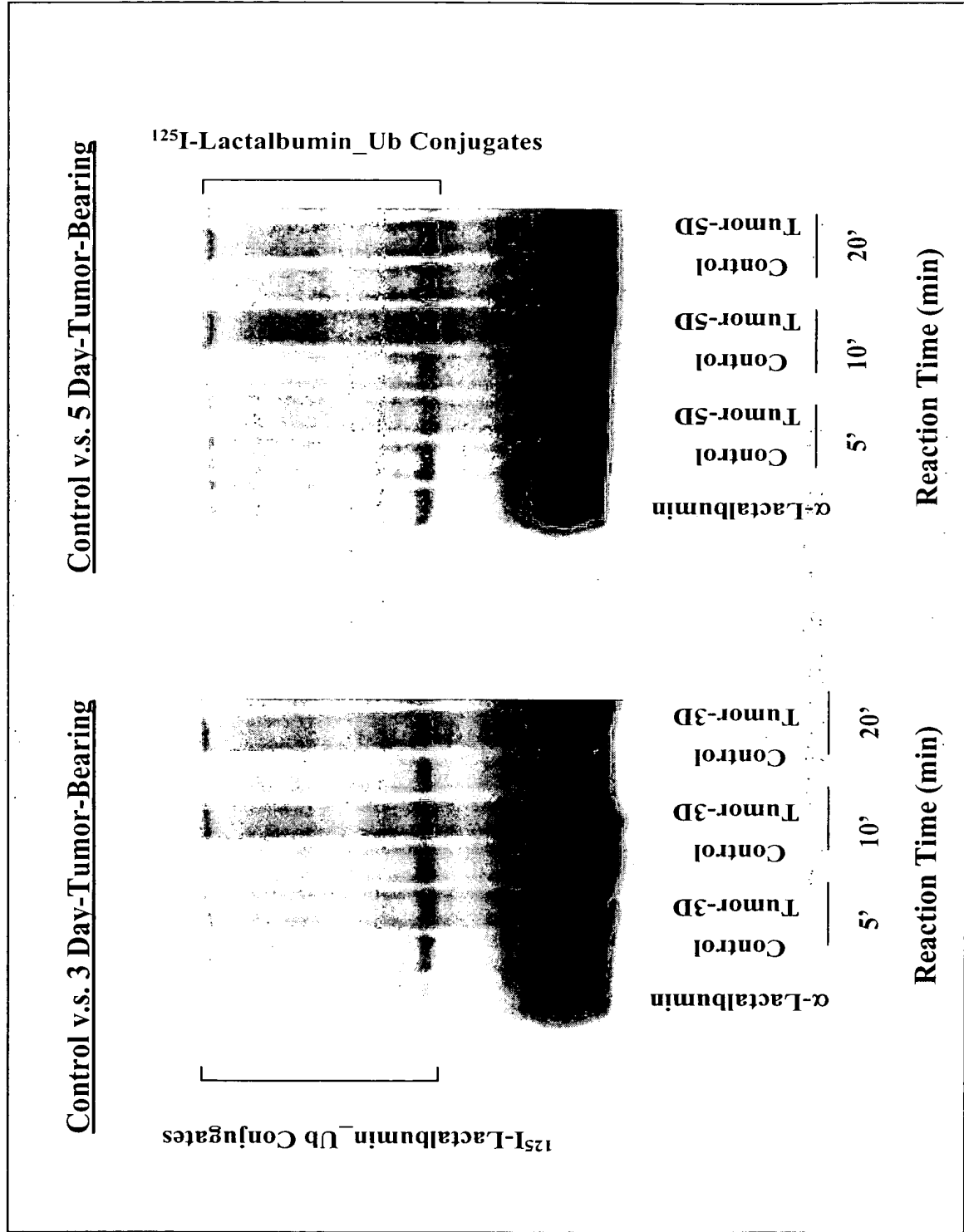
Figure 8

Northern blot analysis of E3α-I & E3α-II expression
in gastrocnemius muscles in YAH-130 exprimental cachexia model

E3α-II

Control, d3   Tumor, d3   Control, d5   Tumor, d5

E3α-I

Control, d3   Tumor, d3   Control, d5   Tumor, d5
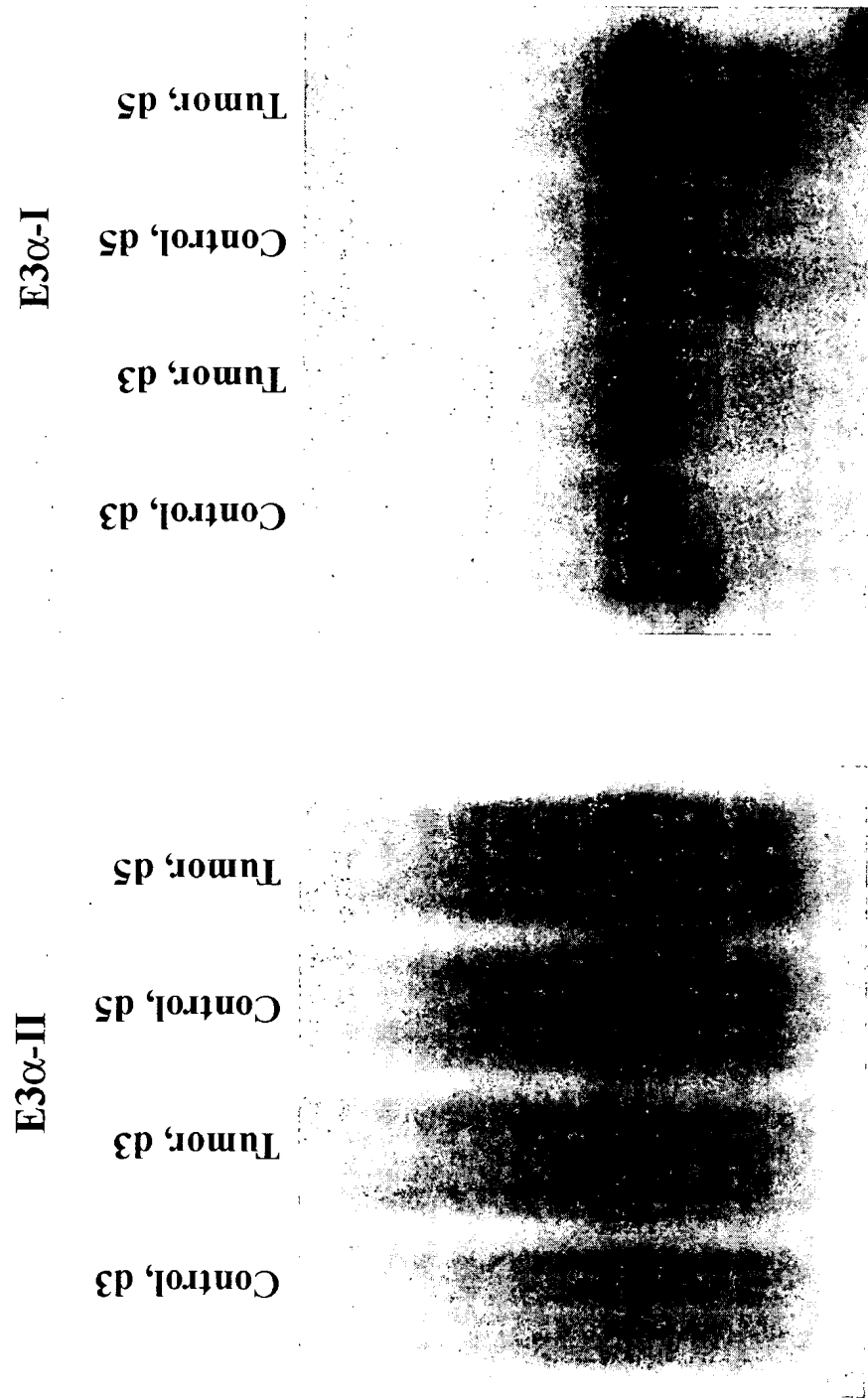
Figure 9

Northern blot analysis of E3α-I and E3α-II expression in gastrocnemius muscle and cardiac muscle in C26 experimental cachexia model
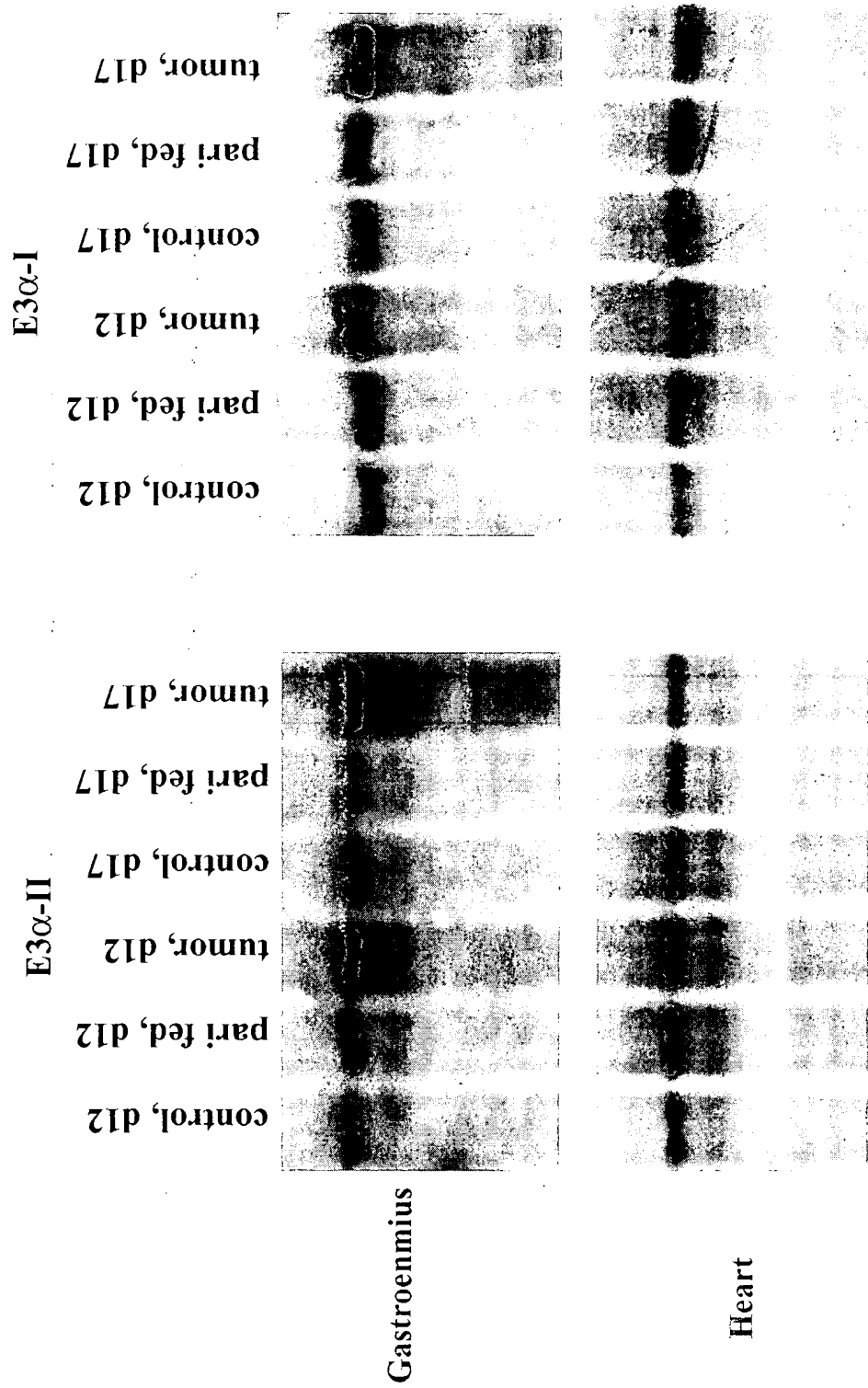
Figure 10

Proinflammatory cytokines TNF-α and IL-6 induce E3α-II Expression in C2C12 myostube culture
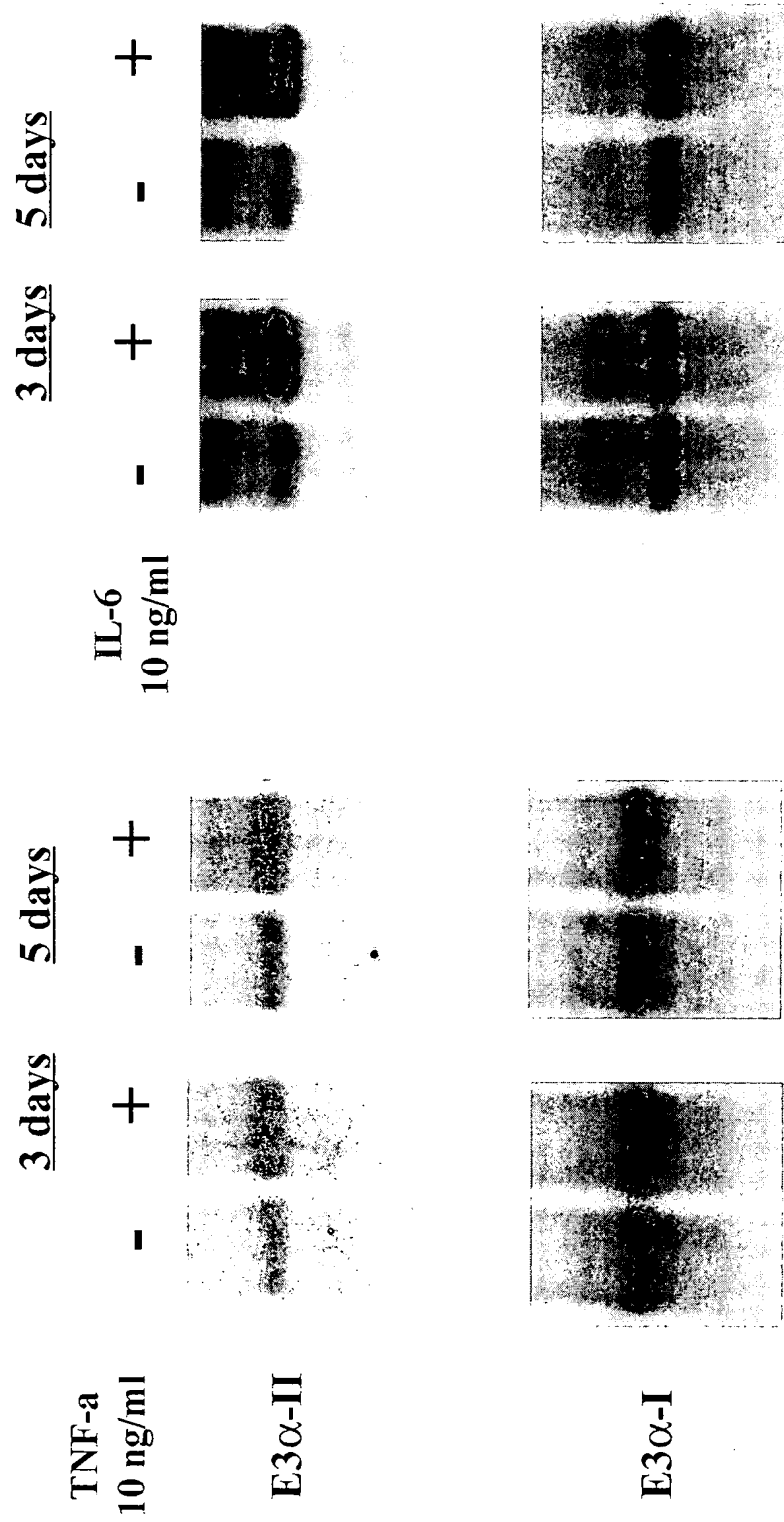
Figure 11

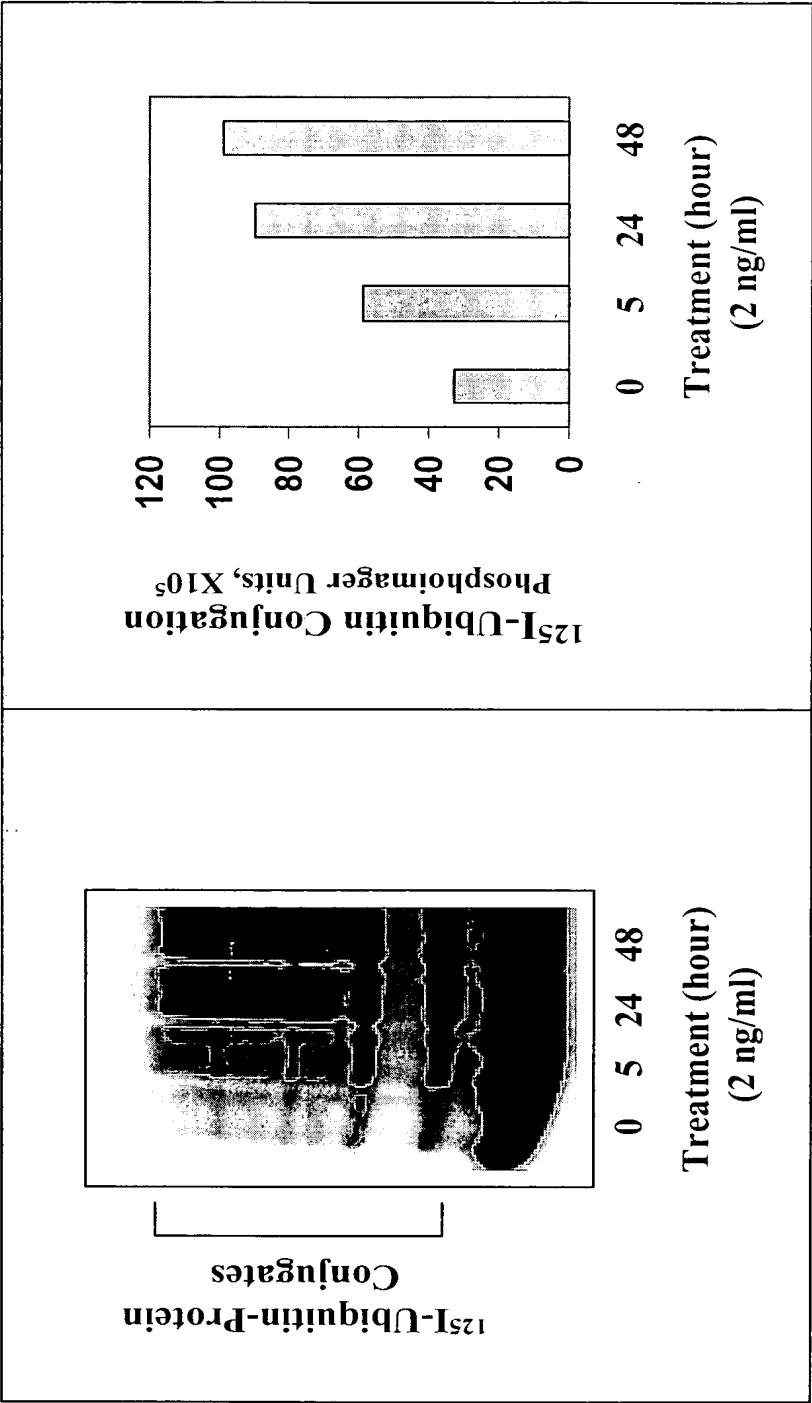# IL-6 Elicits Accelerated Ubiquitination in C2C12 Myotube Cultures

Figure 12

TNFα Elicits Accelerated Ubiquitination in C2C12 Myotube Cultures